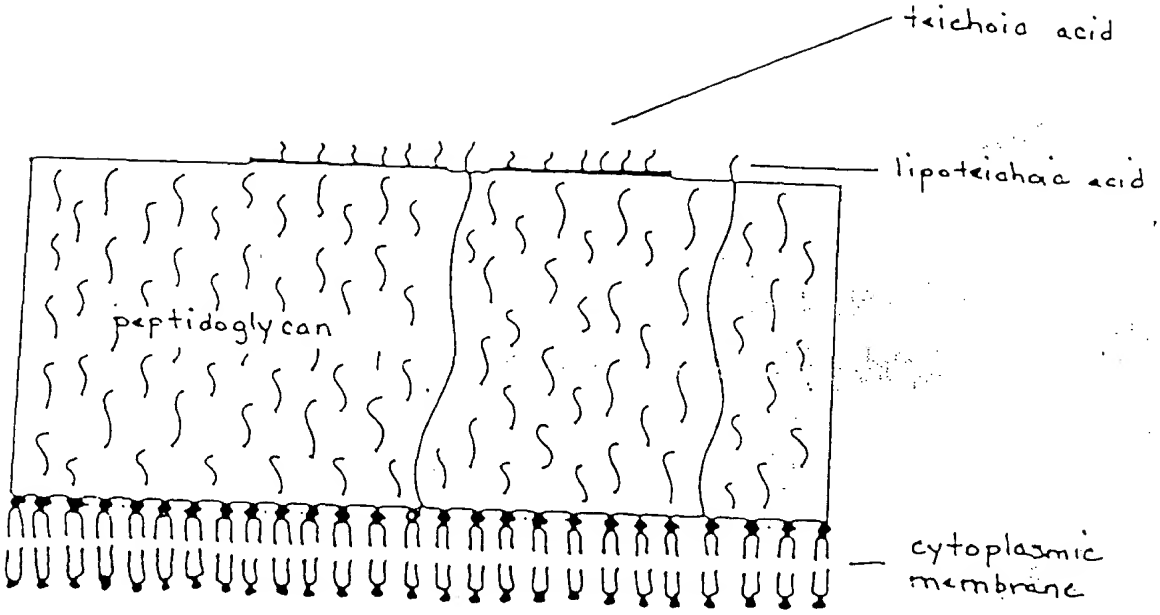
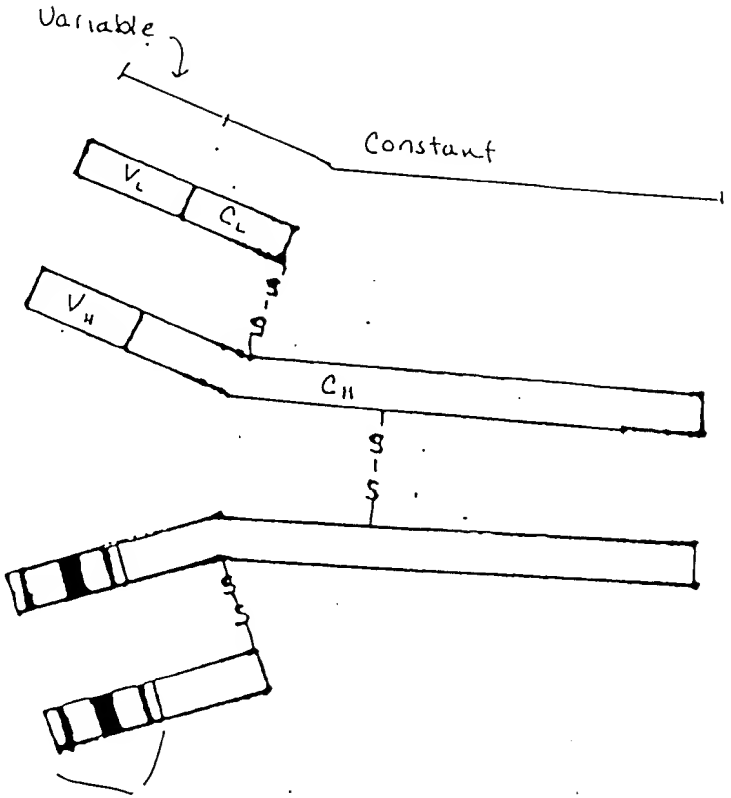
FIGURE 1


teichoic acid
lipoteichoic acid
peptidoglycan
cytoplasmic membrane

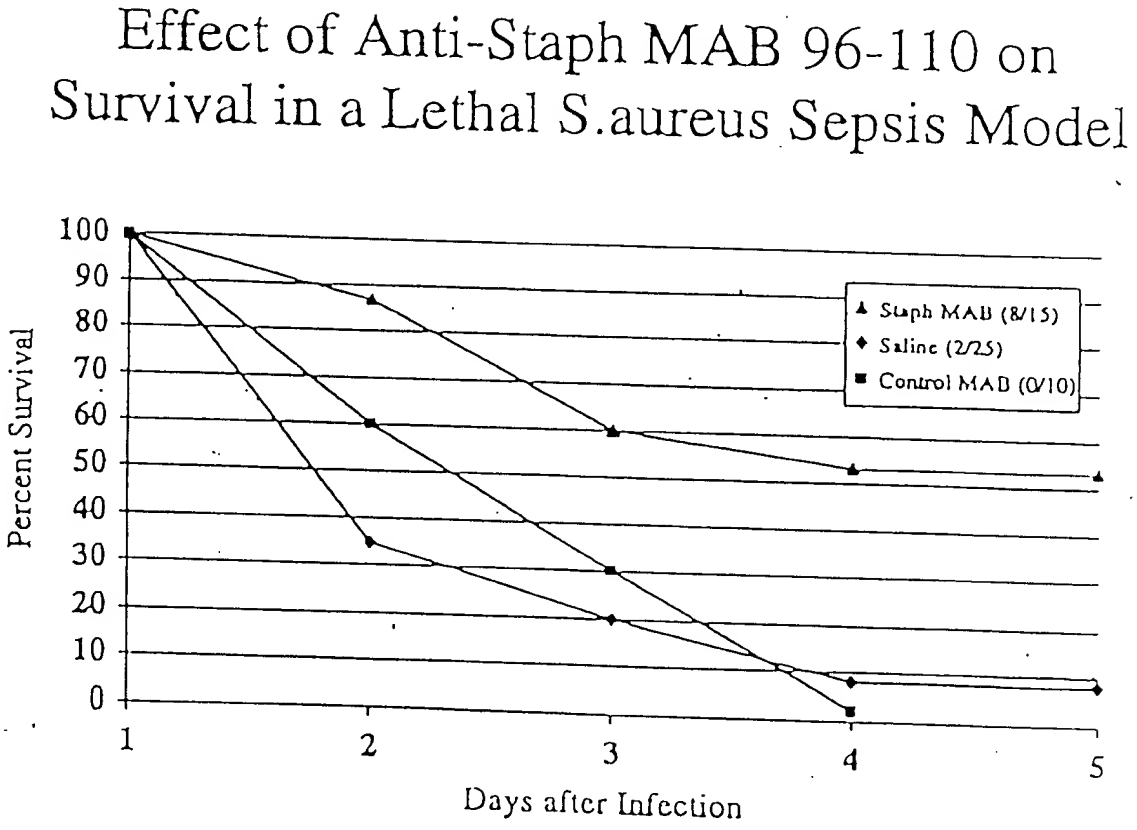
T06290"ST96860

FIGURE 2



Hypervariable regions containing 3 CDRs

FIGURE 3


Effect of Anti-Staph MAB 96-110 on Survival in a Lethal S.aureus Sepsis Model
Percent Survival
100
90
80
70
60
50
40
30
20
10
0
1
2
3
4
5
Days after Infection
Staph MAB (8/15)
Saline (2/25)
Control MAB (0/10)

T06290" ST9E6860

FIGURE 4

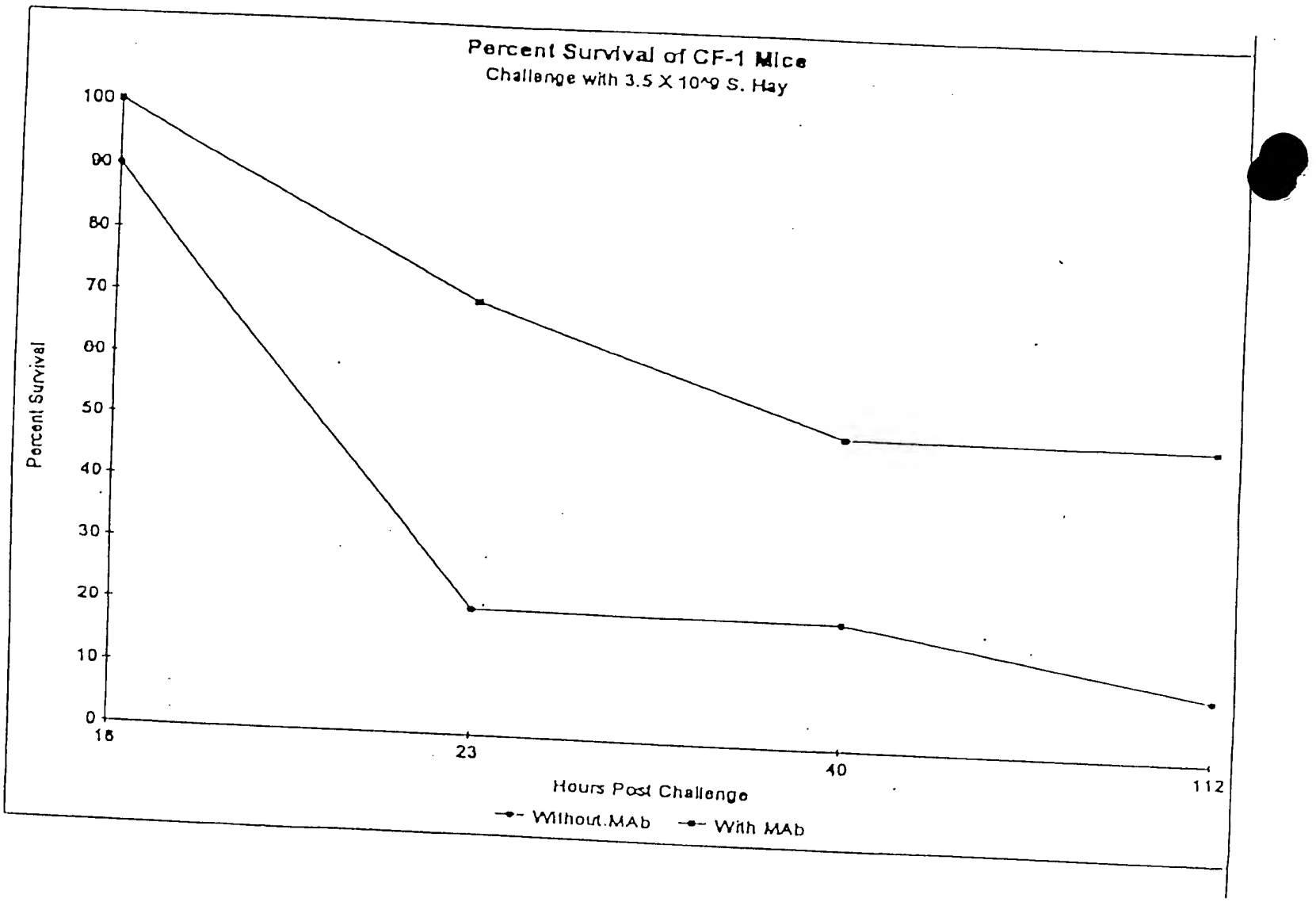
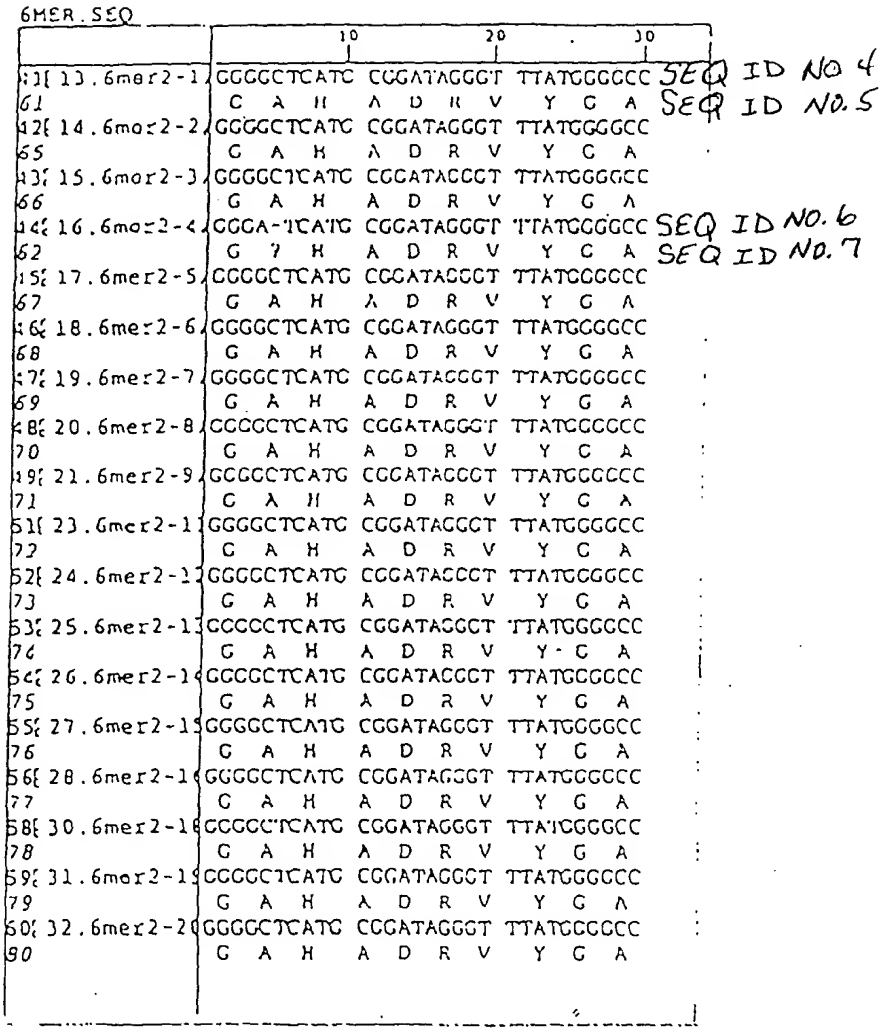


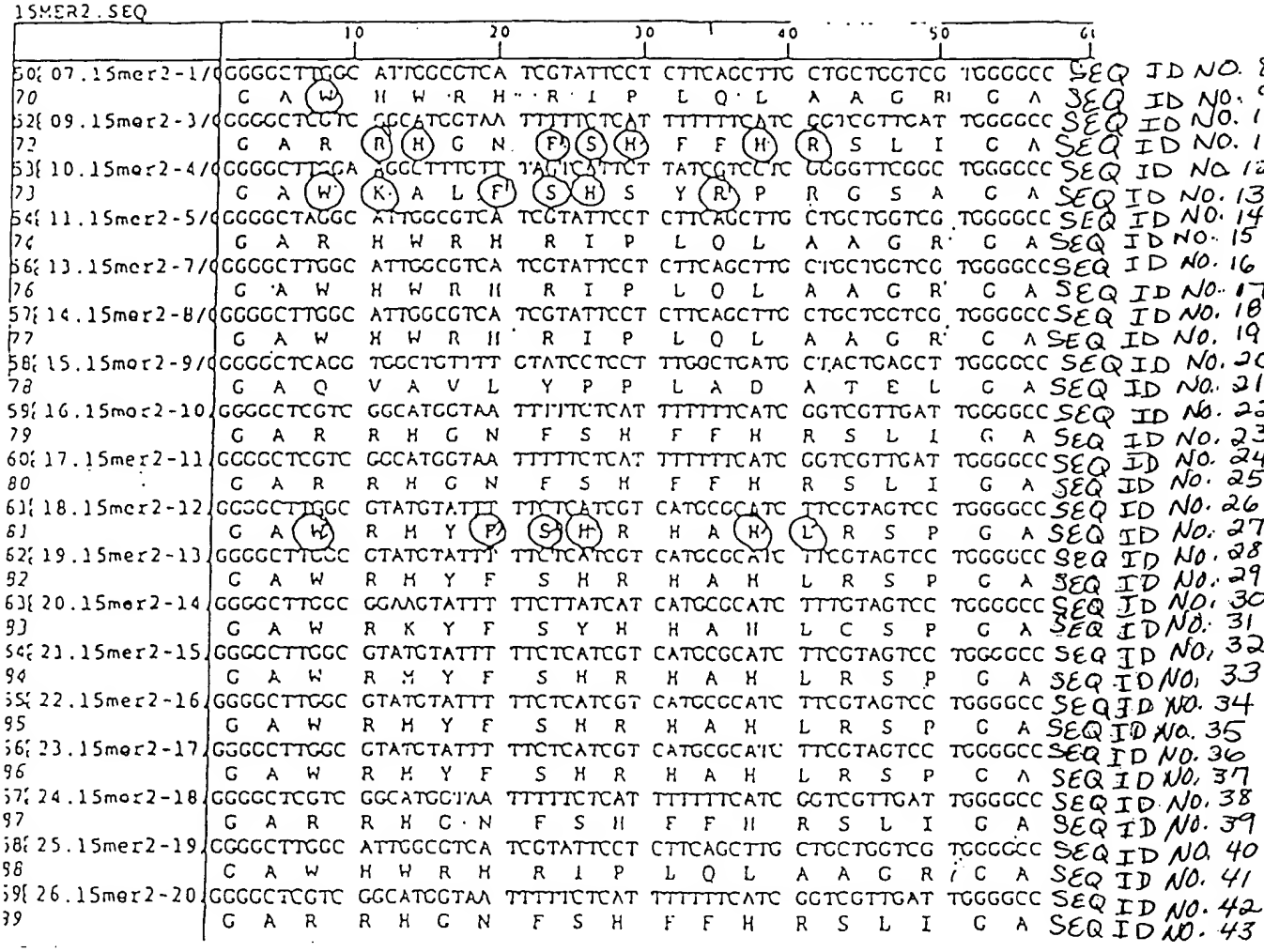
FIGURE 5



SEQ ID NO 4
SEQ ID NO. 5
SEQ ID NO. 6
SEQ ID NO. 7

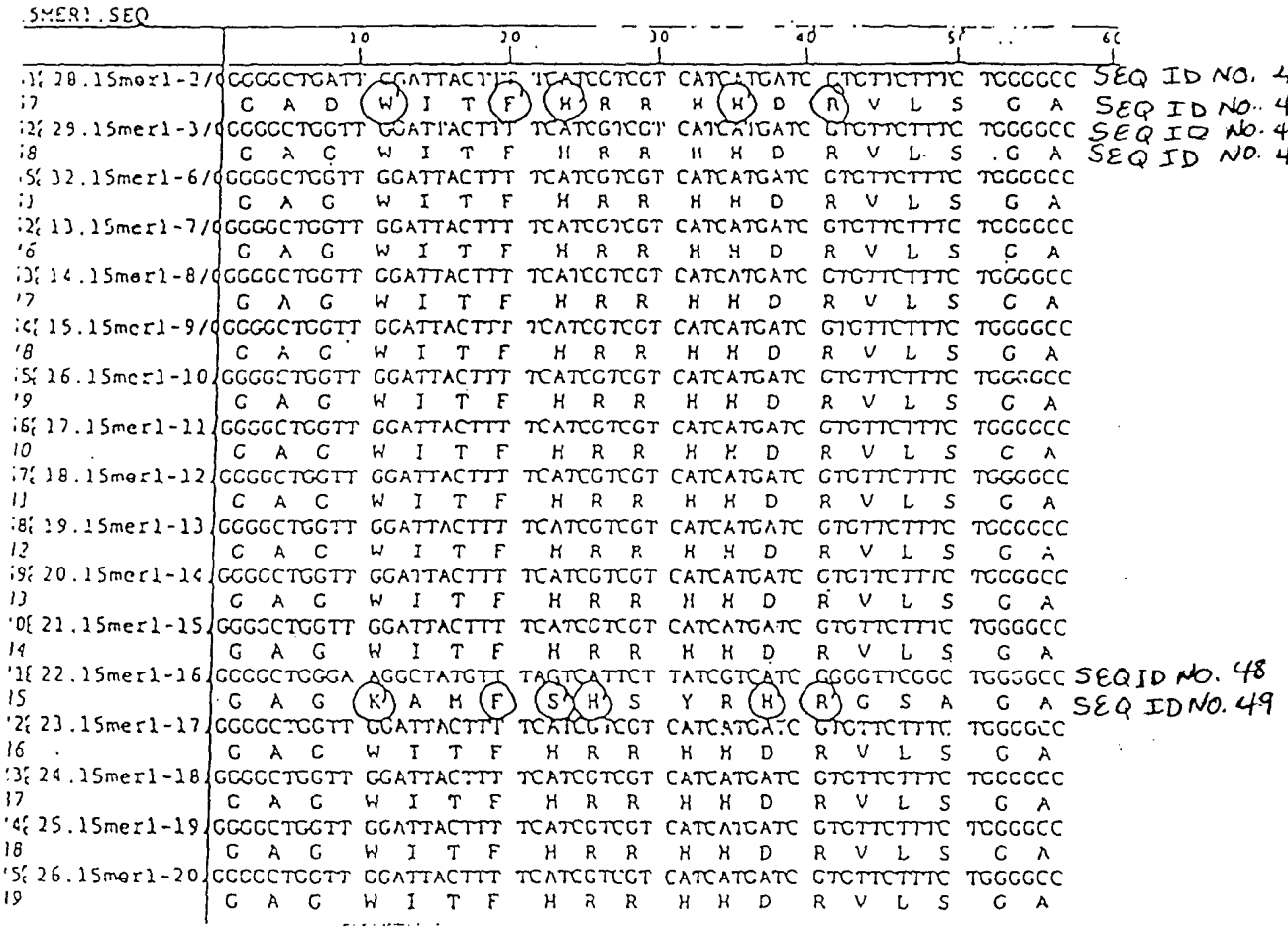
D0G3H5-0G0G0G

FIGURE 6



10-09-03.seq

FIGURE 7



09839615.050501

FIGURE 8

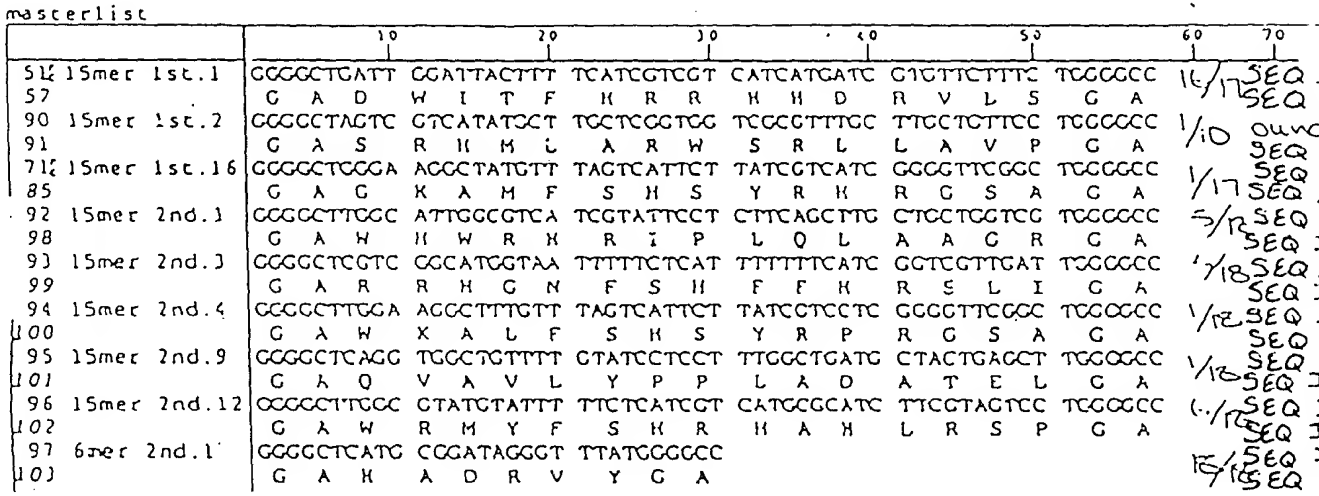

masterlist
10 20 30 40 50 60 70
51 15mer 1st.1 GGGGCTGATT CGATTACTTT TCATCGTCGT CATCATGATC GTGTTCTTTC TCGCGCC 16/17 SEQ ID NO 50
57 G A D W I T F K R R H H D R V L S G A SEQ ID NO 51
90 15mer 1st.2 GGGCCTAGTC GTCATATGCT TGCTCGGTCG TCGCGTTTGC TTGCTGTTCC TCGCGCC 1/10 ound SEQ ID NO 52
91 G A S R K M L A R W S R L L A V P G A SEQ ID NO 53
71 15mer 1st.16 GGGGCTGGGA ACGCTATGTT TAGTCATTCT TATCGTCATC GGCGTTCGGC TCGCGCC SEQ ID NO 54
85 G A G K A M F S H S Y R K R G S A G A 1/17 SEQ ID NO 55
92 15mer 2nd.1 GGGGCTTGGC ATTGGCGTCA TCGTATTCCT CTTCAGCTTG CTGCTGGTCG TCGCGCC 5/18 SEQ ID NO 56
98 G A W K W R K R I P L Q L A A G R G A SEQ ID NO 57
93 15mer 2nd.3 GGGGCTCGTC GGCATGGTAA TTTTTCTCAT TTTTTTCATC GGTCGTTGAT TCGCGCC 1/18 SEQ ID NO 58
99 G A R R H G N F S H F F K R S L I G A SEQ ID NO 59
94 15mer 2nd.4 GGGGCTTTGA AGGCTTTGTT TAGTCATTCT TATCGTCCTC GGGGTTCGGC TCGCGCC 1/18 SEQ ID NO 60
100 G A W X A L F S K S Y R P R G S A G A SEQ ID NO 61
95 15mer 2nd.9 GGGGCTCAGG TGGCTGTTTT GTATCCTCCT TTGGCTGATG CTACTGAGCT TGGCGCC 1/18 SEQ ID NO 62
101 G A Q V A V L Y P P L A D A T E L G A SEQ ID NO 63
96 15mer 2nd.12 GGGGCTTGGC GTATGTATTT TTCTCATCGT CATGCGCATC TTCGTAGTCC TCGCGCC 1/18 SEQ ID NO 64
102 G A W R M Y F S K R H A H L R S P G A SEQ ID NO 65
97 6mer 2nd.1 GGGGCTCATG CGGATAGGGT TTATGGGGCC SEQ ID NO 66
103 G A K A D R V Y G A 15/18 SEQ ID NO 67

FIGURE 9

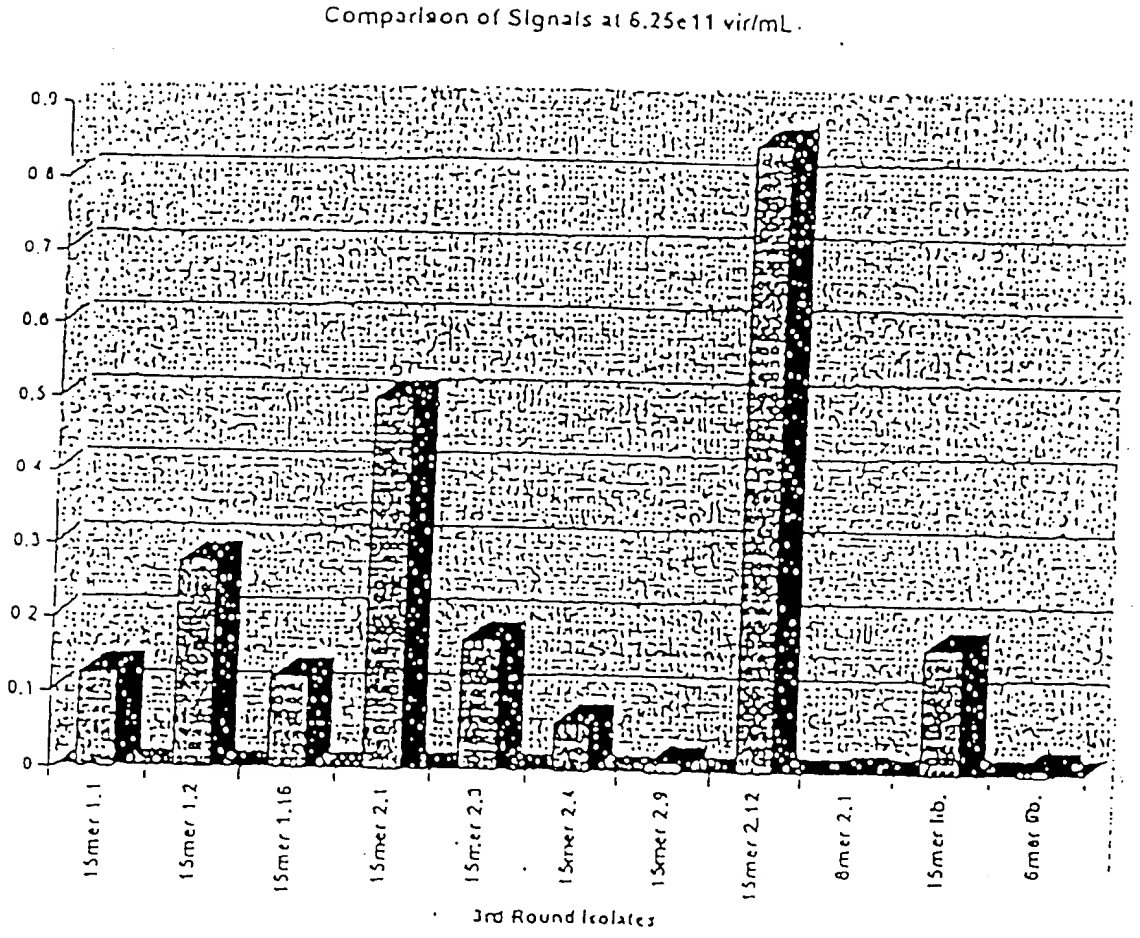

Comparison of Signals at 6.25e11 vir/mL
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
15mer 1.1
15mer 1.2
15mer 1.16
15mer 2.1
15mer 2.3
15mer 2.4
15mer 2.9
15mer 2.12
8mer 2.1
15mer lib.
6mer lib.
3rd Round Isolates

FIGURE 10: General Cloning Strategy

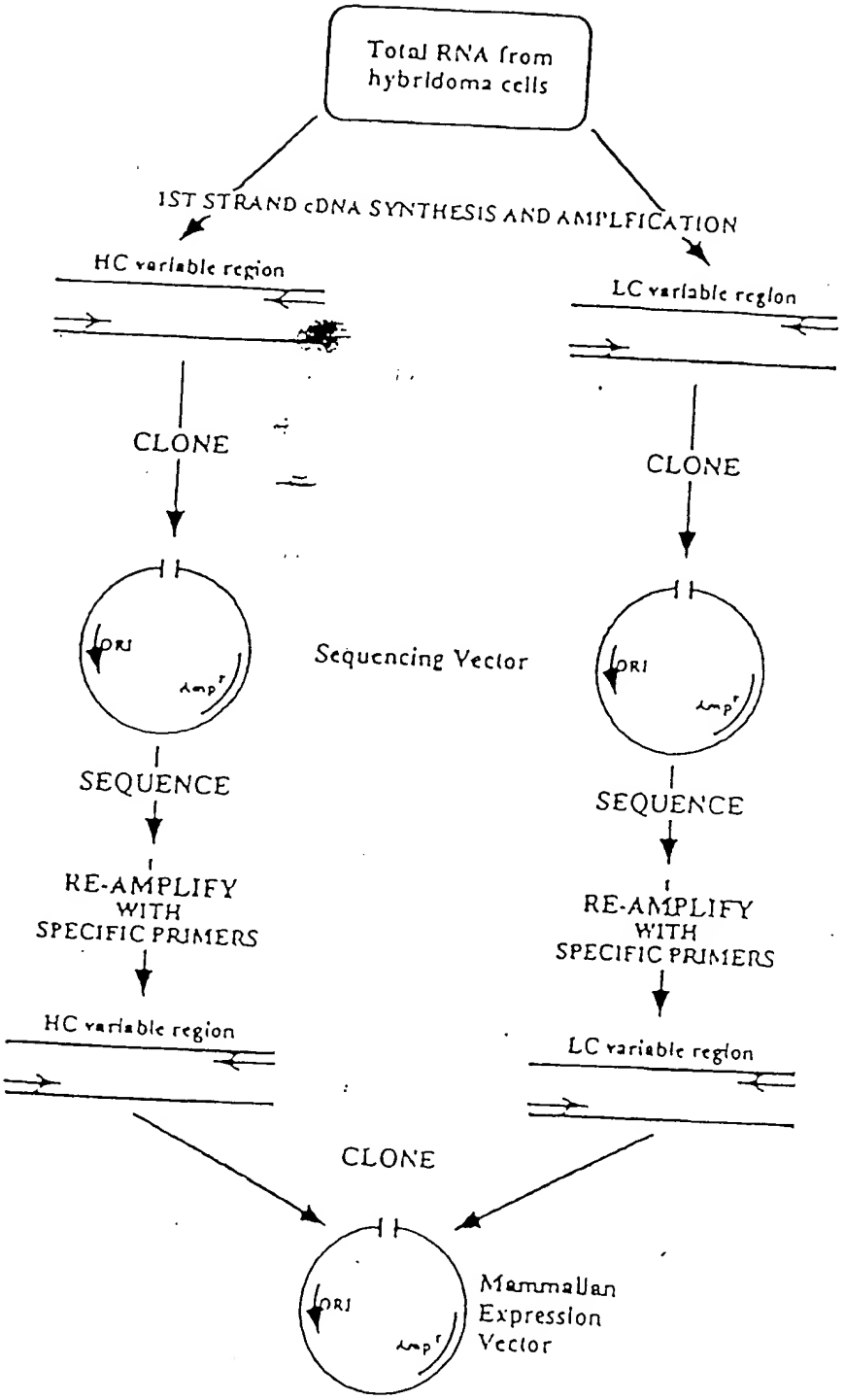


FIGURE 11

Mouse Heavy Chain "front" primers

JSS1
5'-ATTTCAGGCCCAGCCGGCCATGGCCGARGTRMAGCTKSAKGAGWC-3' SEQ ID NO 68
JSS2
5'-ATTTCAGGCCCAGCCGGCCATGGCCGARGTYCARCTKCARCARYC-3' SEQ ID NO 69
JSS3
5'-ATTTCAGGCCCAGCCGGCCATGGCCCAGGTGAAGCTKSTSGARTC-3' SEQ ID NO 70
JSS4
5'-ATTTCAGGCCCAGCCGGCCATGGCCGAVGTGMWGCTKGTGGAGWC-3' SEQ ID NO 71
JSS8
5'-ATTTCAGGCCCAGCCGGCCATGGCCCAGGTBCARCTKMARSARTC-3' SEQ ID NO 72

Mouse Heavy chain "back" primers

JS160
5'-GCTGCCACCGCCACCTGMRGAGACDGTGASTGARG-3' SEQ ID NO 73
JS161
5'-GCTGCCACCGCCACCTGMRGAGACDGTGASMGTRG-3' SEQ ID NO 74
JS162
5'-GCTGCCACCGCCACCTGMRGAGACDGTGASCAGRG-3' SEQ ID NO 75

Mouse Light Chain Leader "front" primers

PMC12
5'-CCCGGGCCACCATGGAGACAGACACACTCCTG-3' SEQ ID NO 76
PMC13
5'-CCCGGGCCACCATGGATTTTCAAGTGCAGATTTTC-3' SEQ ID NO 77
PMC14
5'-CCCGGGCCACCATGGAGWCACAKWCTCAGGTC-3' SEQ ID NO 78
PMC15
5'-CCCGGGCCACCATGKCCCCWRCTCAGYTTCTKG-3' SEQ ID NO 79
PMC55
5'-CCCGGGCACCATGAAGTTGCCTGTTAGGCTG-3' SEQ ID NO 80

Mouse Light Chain "back" primer

OKA57
5'-GCACCTCCAGATGTTAACTGCTC-3' SEQ ID NO 81

"96-110" Specific Primers

96110HF2
5'-TAATATCGCGACAGCTACAGGTGTCCACTCCCGAAGTGATGCTGGTGGAGWCTG-3' SEQ ID NO 82
96110HB
5'-TTATAGAATTCTGAGGAGACGGTGAGTGAG-3' SEQ ID NO 83
96110BLF
5'-TTAGGCGATATCGTTCTCTCCCAGTCTCC-3' SEQ ID NO 84
96110BLB
5'-GTAACCGTTCGAAAAGTGTACTTACGTTTTATTTCCAGCATGGTCC-3' SEQ ID NO 85

Docket No. 0609.4US.00

FIGURE 12

96-110 anti-staph (HAY) heavy chain variable region (type IIIA)

GAAGTGATGCTGGTGGAGTCTGGTGGAGGATTGGTGCAGCCTAAAGGGTCATTGAAACTCTCATGTGCAGCCTCTGGATTCACCTTCAAT SEQ ID NO. 86
E V M L V E S G G G L V Q P K G S L K L S C A A S G F T F N SEQ ID NO. 7

AACTACGCCATGAAT TGGGTCCGCCAGGCTCCAGGAAAGGGTTTGGAATGGGTTGCT SEQ ID NO. 88
N Y A M N W V R Q A P G K G L E W V A SEQ ID NO. 89

CGCATAAGAAGTAAAAGTAATAATTATGCAACATTTTATGCCGATTCAGTGAAAGAC SEQ ID NO. 90
R I R S K S N N Y A T F Y A D S V K D SEQ ID NO. 91

AGGTTCACCATCTCCAGAGATGATTCACAAAGCATGCTCTATCTGCAAATGAACAACTTGAAAACTGAGGACACAGCCATGTATTACTGTGTGAGA SEQ ID NO.
R F T I S R D D S Q S M L Y L Q M N N L K T E D T A M Y Y C V R SEQ ID NO. 9

CGGGGGGCTTCAGGGATTGACTATGCTATGGACTAC TGGGGTCAAGGAACCTCACTCACCGTCTCCTCA SEQ ID NO. 94
R G A S G I D Y A M D Y W G Q G T S L T V S S SEQ ID NO. 95

96-110 anti-staph (HAY) light chain variable region (type VI)

CAAATTGTTCTCTCCCAGTCTCCAGCAATCCTGTCTGCATCTCCAGGGGAAAAGGTCACAATGACTTGC SEQ ID NO. 96
Q I V L S Q S P A I L S A S P G E K V T M T C SEQ ID NO. 97

AGGGCCAGCTCAAGTGTAAATTACATGCAC SEQ ID NO. 98
R A S S S V N Y M H SEQ. ID NO. 99

TGGTACCAGCAGAAGCCAGGATCCTCCCCCAAACCCTGGATTTCT GCCACATCCAACCTGGCTTCT SEQ ID NO. 100
W Y Q Q K P G S S P K P W I S A T S N L A S SEQ ID NO. 101

GGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACCTCTTACTCTCTCACAATCAGCAGAGTGGAGGCTGAAGATGCTGCCACTTATTACTGC SEQ ID NO.10
G V P A R F S G S G S G T S Y S L T I S R V E A E D A A T Y Y C SEQ ID NO. 103

CAGCAGTGGAGTAGTAACCCACCCACG TTCGGAGGGGGGACCATGCTGGAAATAAGA SEQ ID NO. 104
Q Q W S S N P P T F G G G T M L E I R SEQ ID NO. 105

CDR Regions Underlined

FIGURE 13

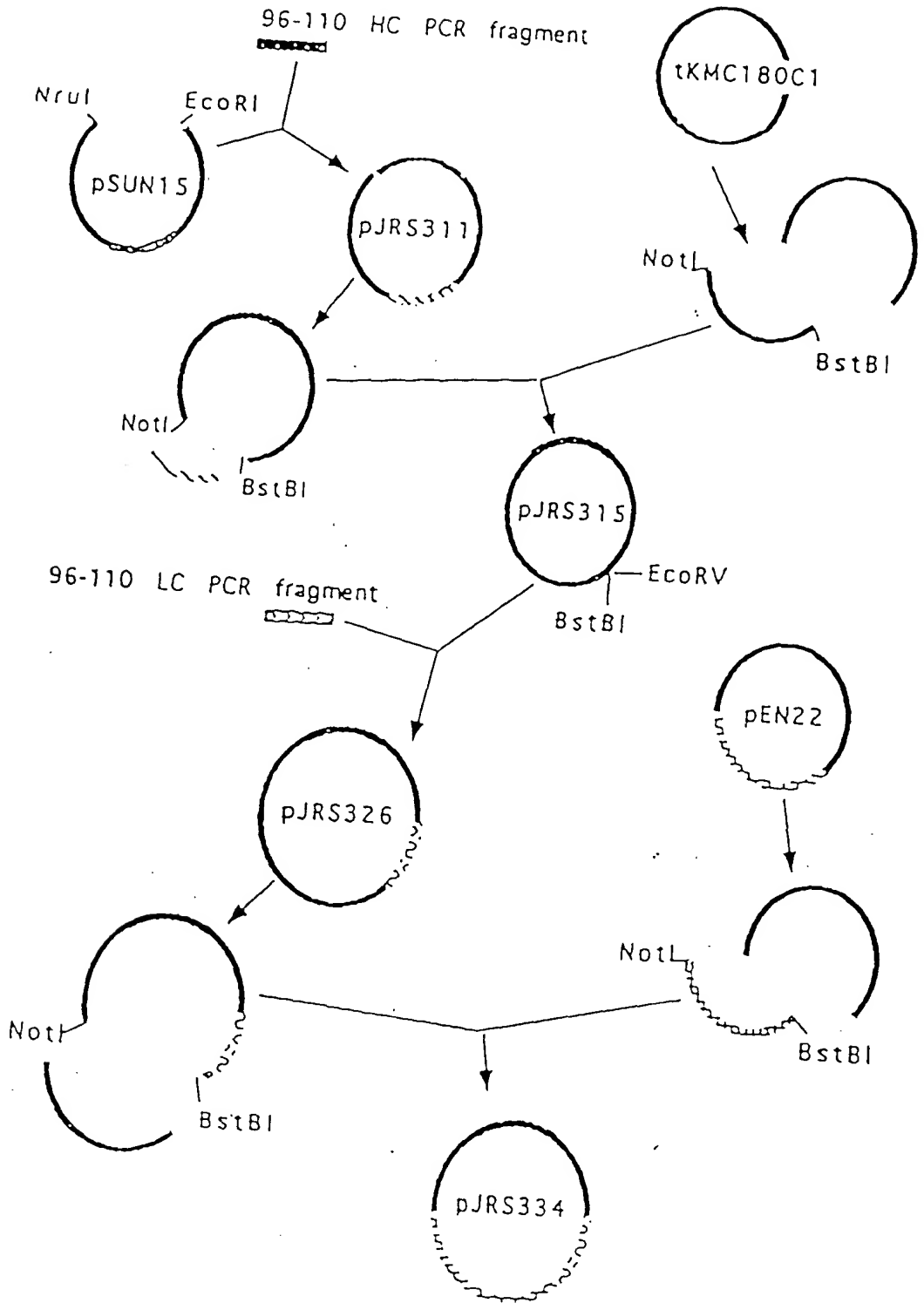
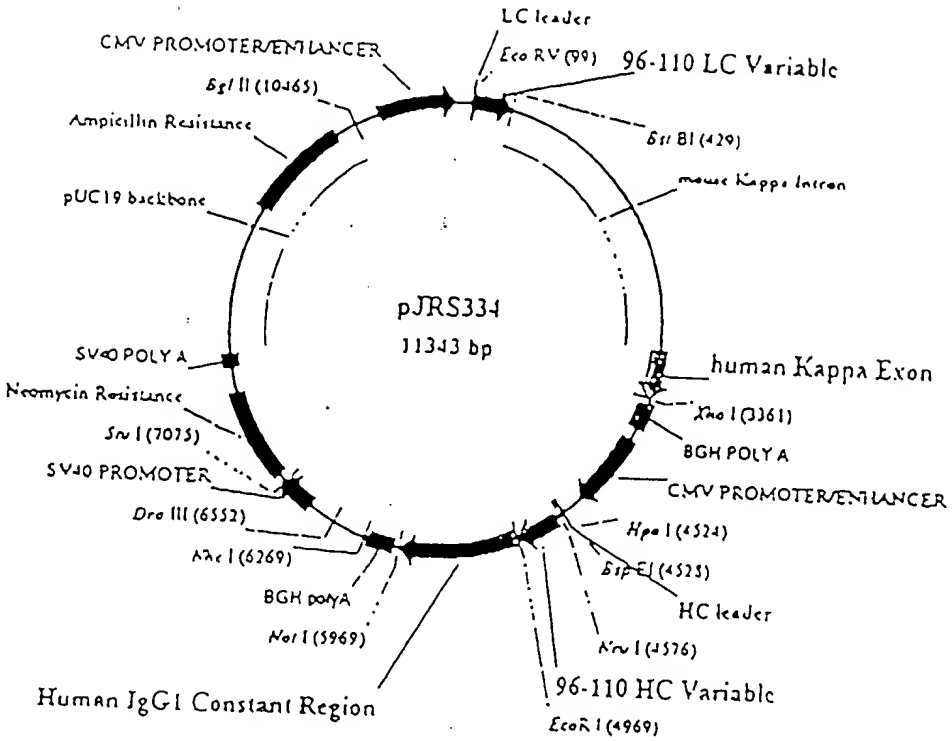

96-110 HC PCR fragment
NruI
EcoRI
pSUN15
pJRS311
tKMC180C1
NotI
BstBI
NotI
BstBI
pJRS315
EcoRV
BstBI
96-110 LC PCR fragment
pEN22
pJRS326
NotI
BstBI
NotI
BstBI
pJRS334

FIGURE 14



Common Unique Restriction Sites Shown

PCT/US2005/045350

T06290 ST9E6860

FIGURE 15: Antibody Production ELISA

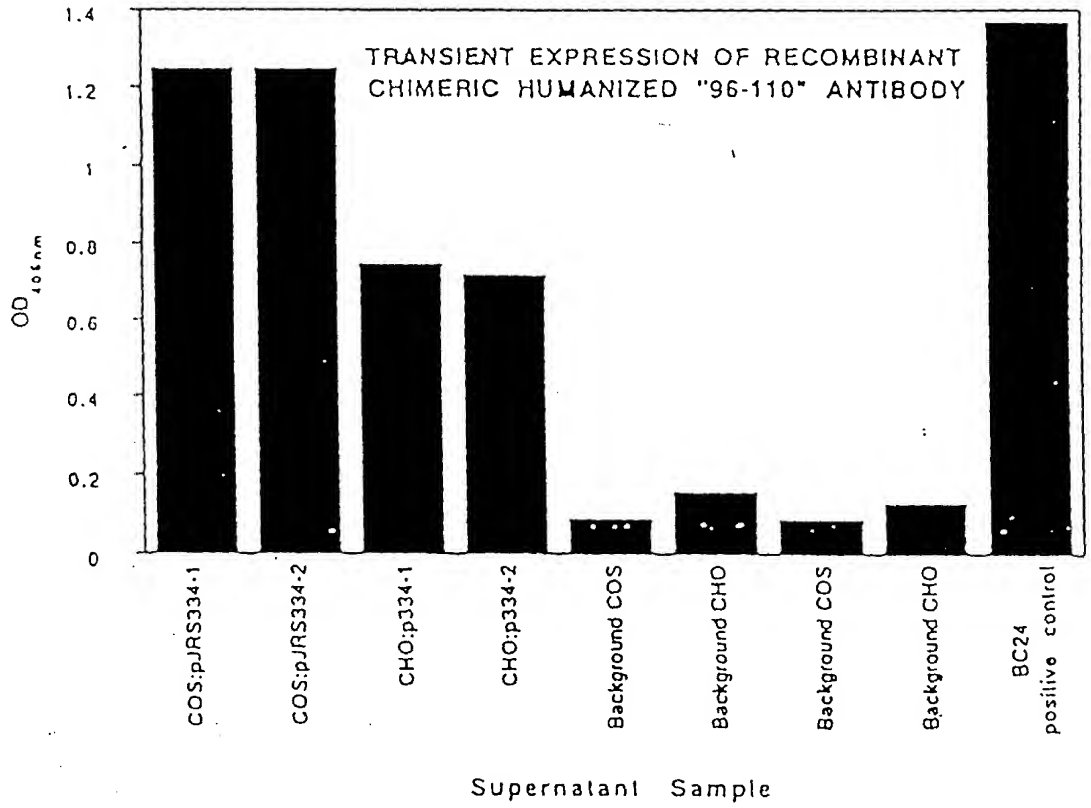


FIGURE 16: Anti-Staph HAY Activity ELISA

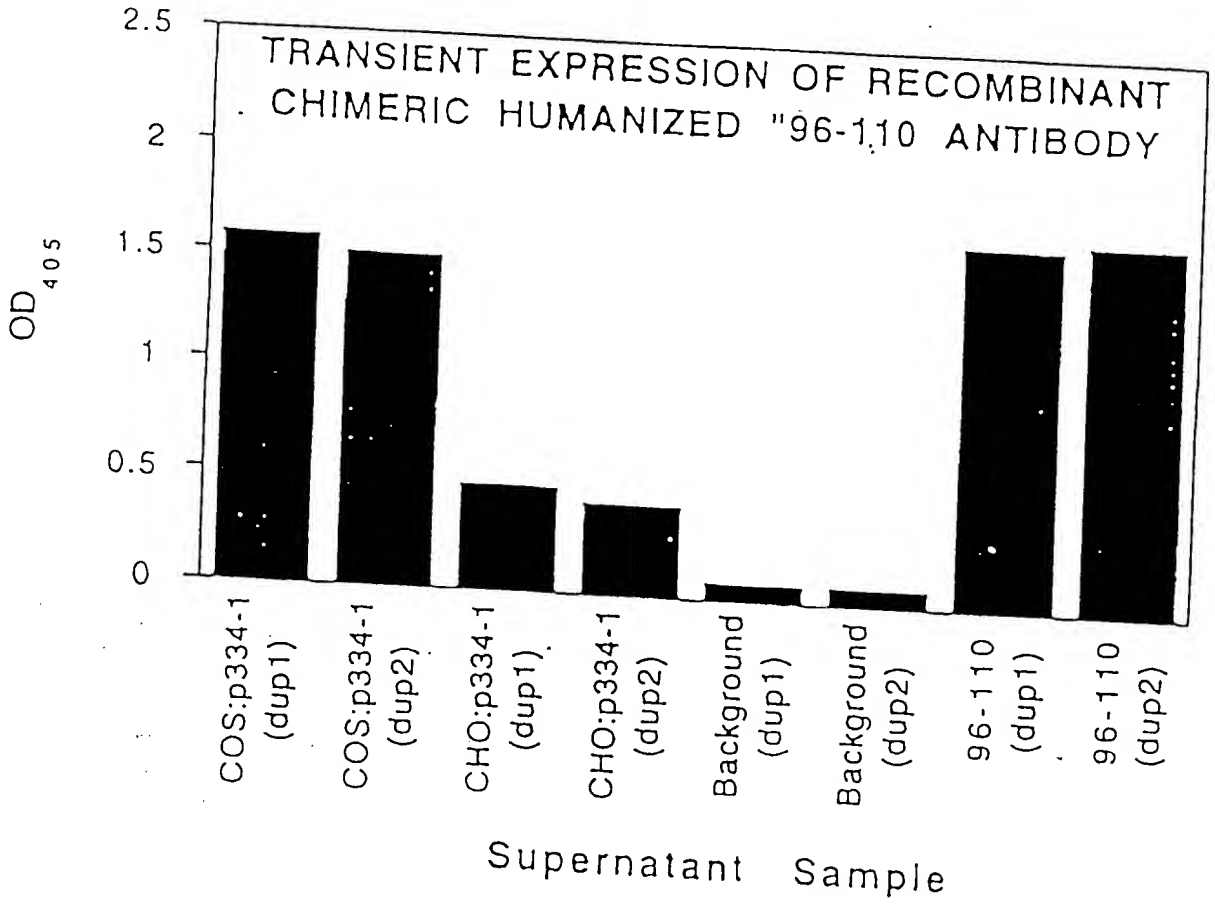
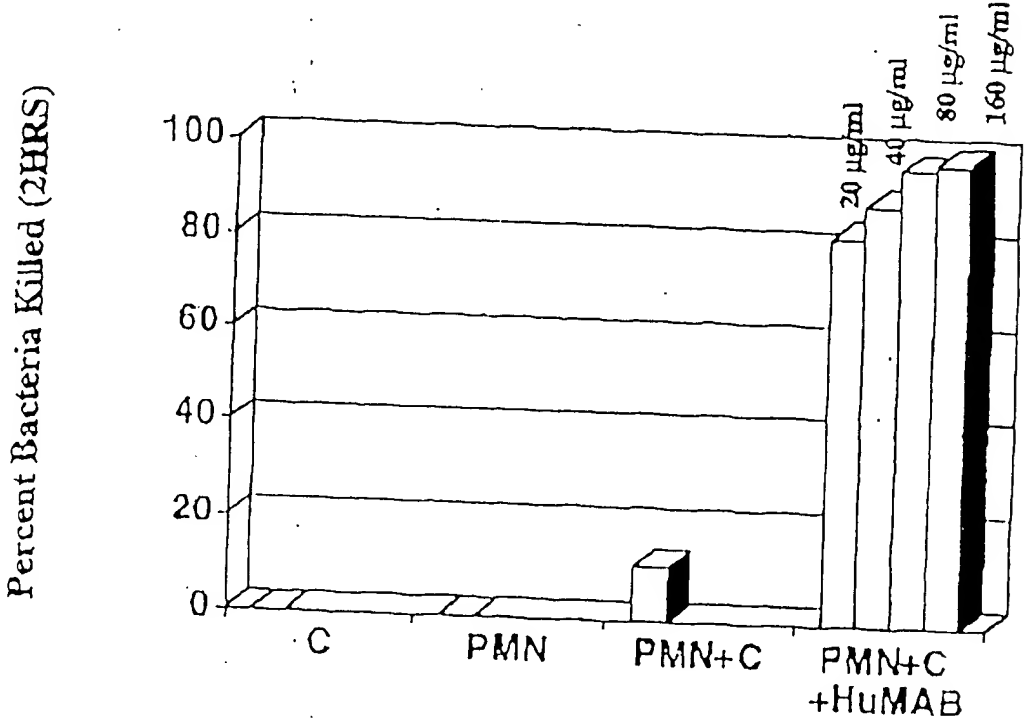


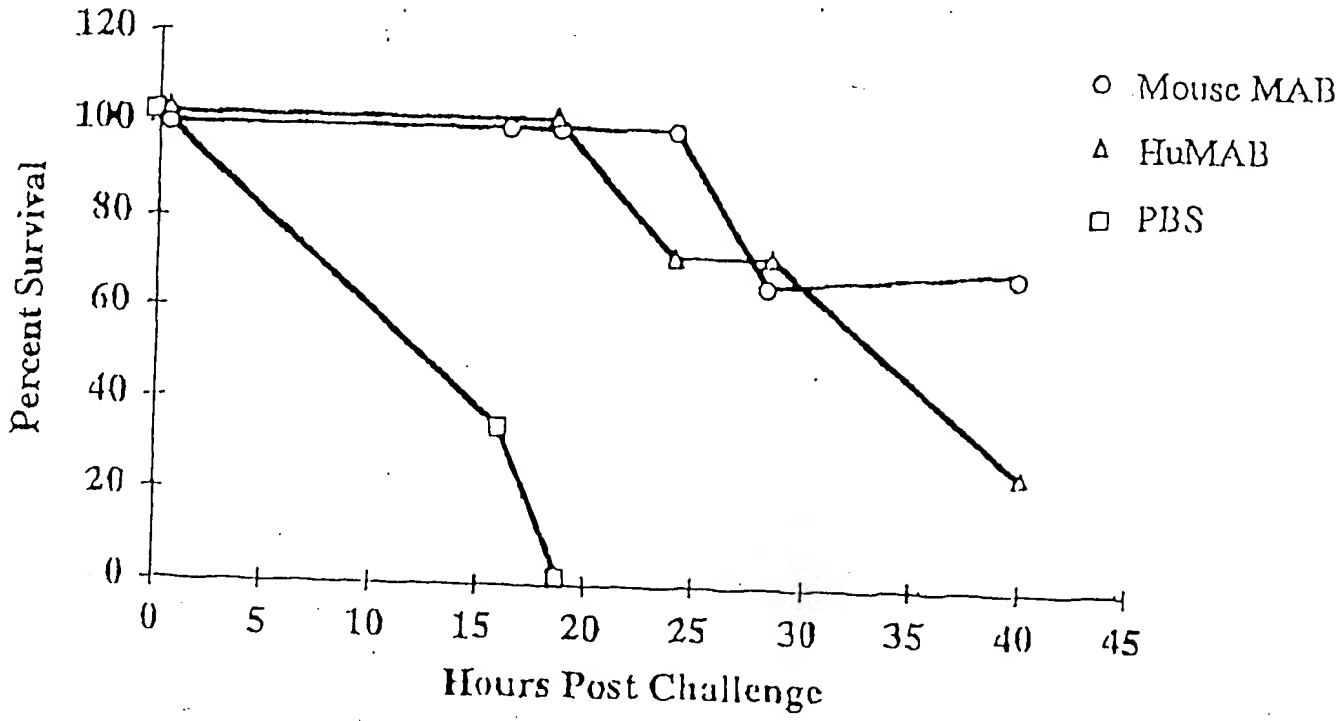
FIGURE 17

Opsonic Activity of HuMAB 96-110 for *S.epidermidis* in a Neutrophil Mediated Opsonophagocytic Bactericidal Assay Using Human Complement



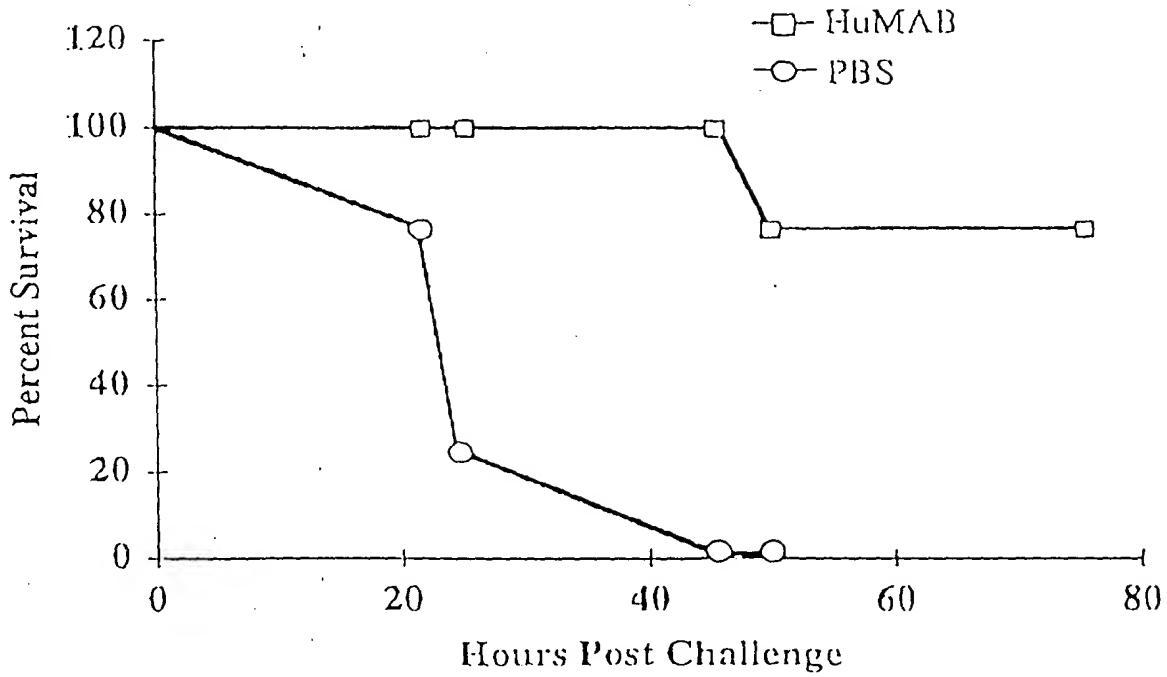
C-Barb-Ex (1:4), Human
PMN-Human
Bacterin-*S.epidermidis* (Strain Hay)

Pilot Study to Compare the Effect of Mouse MAB 96-110 and HuMAB 96-110 in a Lethal Model of *S. Epidermidis* Sepsis



MAB dose: 14 mg/kg given IP, 24 and 1 Hour prior to infection

Survival of CF-1 Mice after Intraperitoneal Challenge with $3x10^9$ *S. epidermidis* (Hay)



18 mg/kg/dose, IP, 24 and 1 Hour prior to infection

Effect of HuMAB 96-110 on Bacteremia in a Lethal *S. epidermidis* Sepsis Model

Geometric Mean Bacteremia Level

Saline Placebo	6.5×10^4	7.2×10^4	5.2×10^4	7×10^3
HuMAB 96-110	3×10^2	7.5×10^2	2.1×10^1	1.7×10^1
	4 hrs	8 hrs	12 hrs	18 hrs

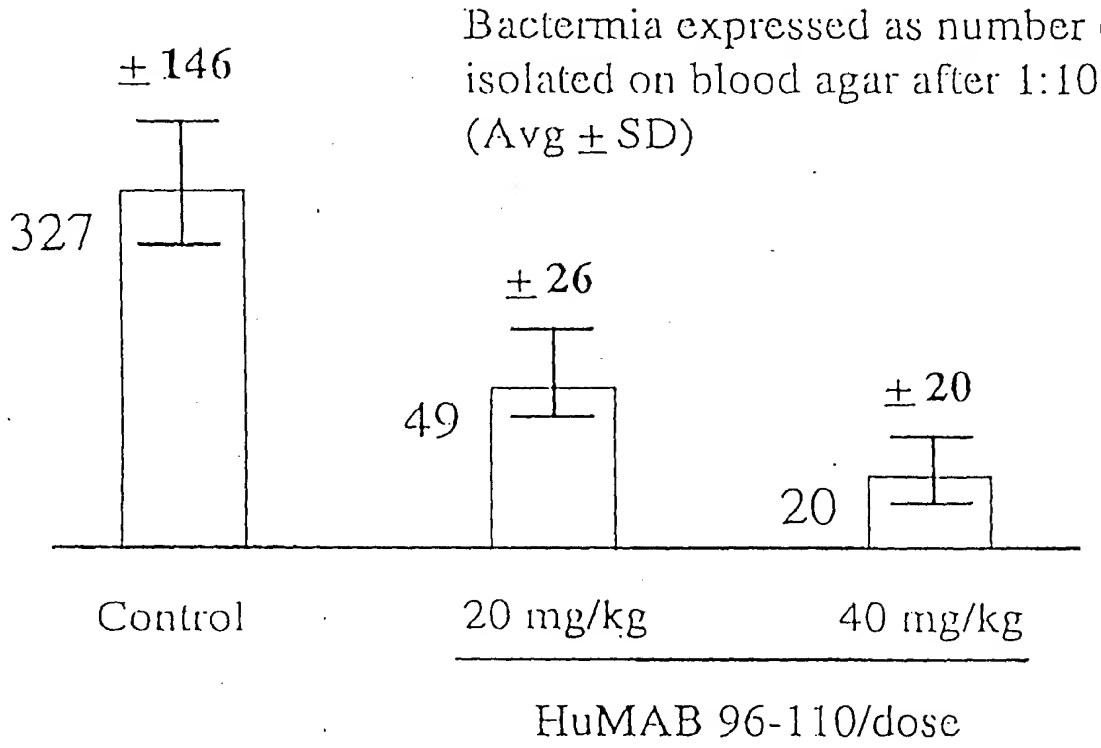
Time Post Infection

HuMAB 96-110 18 mg/kg/dose or saline given IP, 24 and 1 hour prior to IP infection with 3×10^9 *S. epidermides* (Hay)

T06290 ST3E6B50

FIGURE 21

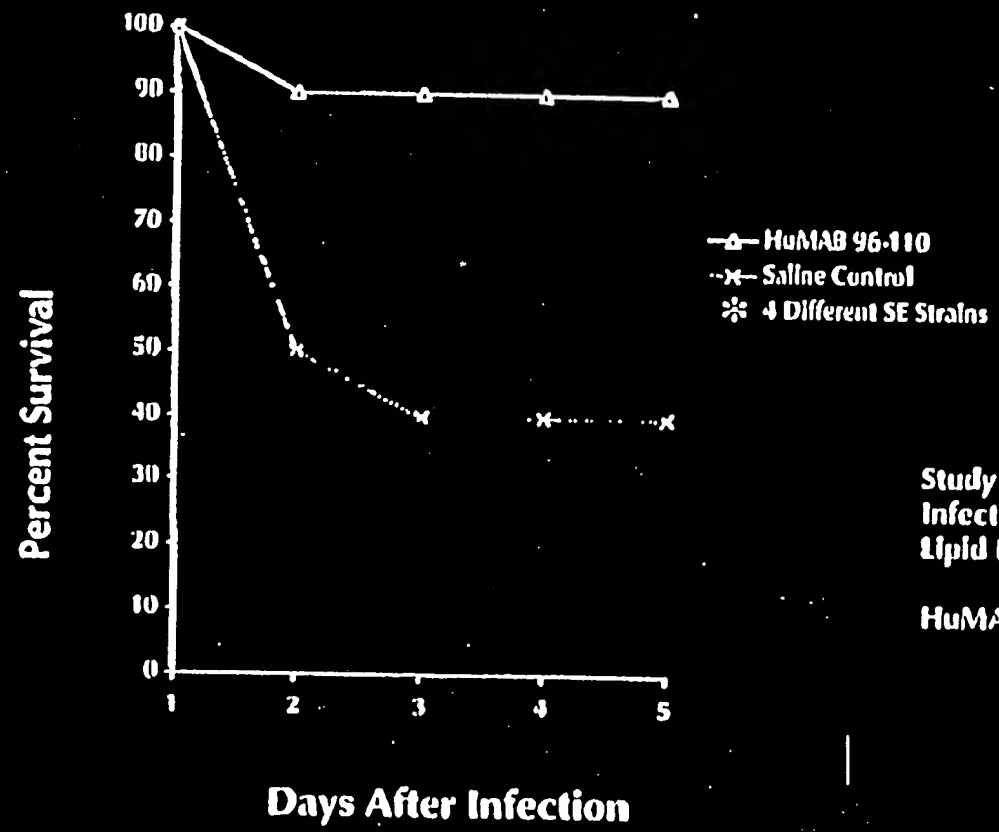
Bacteremia levels 4 hrs after infection with 3 x 10^9 *S.epidermidis**



* CF-1 mice infected IP with strain Hay-HuMAB given IP x 2

FIGURE 22

The Effect of Hu 96-110 on Survival in a Lethal Neonatal *S.epidermidis** Sepsis Model: Study II



Survival:
Hu 96-110 27/30 (90%)
Saline 12/30 (40%)

Study II:
Infection- ~5x10⁷ SE, SQ (with plastic catheter SQ)
Lipid Emulsion - 0.2 ml, 20% IP day-1 and + 1, 2 doses day 0
HuMAB or Saline- 0.2 ml, IP 30 min before and 24 hrs after infection
Dose; 50-60 mg/kg per dose

SCANNED,# 20

FIGURE 12

96-110 anti-staph (HAY) heavy chain variable region (type IIIA)

GAAGTGATGCTGGTGGAGTCTGGTGGAGGATTGGTGCAGCCTAAAGGGTCATTGAAACTCTCATGTGCAGCCTCTGGATTCACCTTCAAT
E V M L V E S G G G L V Q P K G S L K L S C A A S G F T F N

AACTACGCCATGAAT TGGGTCCGCCAGGCTCCAGGAAAGGGTTTGGAATGGCTTGCT
N Y A M N W V R Q A P G K G L E W V A

CGCATAAGAAGTAAAAGTAATAATTATGCAACATTTTATGCCGATTCAGTGAAAGAC
R I R S K S N N Y A T F Y A D S V K D

AGGTTCACCATCTCCAGAGATGATTCACAAAGCATGCTCTATCTGCAAATGAACAACTTGAAAACTGAGGACACAGCCATGTATTACTGTGTGAGA
R F T I S R D D S Q S M L Y L Q M N N L K T E D T A M Y Y C V R

CGGGGCGGCTTCAGGGATTGACTATGCTATGGACTAC TGGGGTCAAGGAACCTCACTCACCGTCTCCTCA SEQ ID NO. 86
R G A S G I D Y A M D Y W G Q G T S L T V S S SEQ ID NO. 87

96-110 anti-staph (HAY) light chain variable region (type VI)

CAAATTGTTCTCTCCCAGTCTCCAGCAATCCTGTCTGCATCTCCAGGGGAAAAGGTCACAATGACTTGC
Q I V L S Q S P A I L S A S P G E K V T M T C

AGGGCCAGCTCAAGTGTAAATTACATGCAC
R A S S S V N Y M H

TGGTACCAGCAGAAGCCAGGATCCTCCCCCAAACCCTGGATTTCT GCCACATCCAACCTGGCTTCT
W Y Q Q K P G S S P K P W I S A T S N L A S

GGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACCTCTTACTCTCTCACAATCAGCAGAGTGGAGGCTGAAGATGCTGCCACTTATTACTGC
G V P A R F S G S G S G T S Y S L T I S R V E A E D A A T Y Y C

CAGCAGTGGAGTAGTAACCCACCCACG TTCGGAGGGGGGACCAAGCTGGAAATAAGA SEQ ID NO. 88
Q Q W S S N P P T F G G G T K L E I R SEQ ID NO. 89

CDR Regions Underlined